REMARKS

Reconsideration of the present Application is respectfully requested. Claims 1-7, 10, and 22 are pending in the Application. Claims 1, 3-4, and 10 have been amended and new claim 23 has been added to define more clearly an embodiment of Applicants' invention. Support for the amended claims and new claim may be found in the specification, for example, at page 19, lines 16-21. No new subject matter has been added.

Applicants respectfully submit, as noted above, that the present Amendment adds no new subject matter beyond the Application as originally filed. The specification teaches that disseminated tumor cells may be isolated from body fluids free from a separating agent that is a ligand used for isolation of cancer cells, which ligand may be an antibody or a lectin or the like (page 19, lines 16-21). The disseminated tumor cells are thus in a biological state and not in an artificial state that may occur as a result of, for example, fixing or labeling the cells (page 19, lines 21-39) or attaching the cells to a construct such as glass beads (page 5, lines 14-26). Accordingly, Applicants respectfully request reconsideration of the present Application in view of the present Amendments and the following Remarks.

OBJECTIONS TO THE CLAIMS

The PTO objects to claims 4 and 5 under 37 C.F.R. § 1.75(c), alleging that the claims are multiple dependent claims that depend upon other multiple dependent claims and thus are in improper form. Consequently, claims 4 and 5 have not been examined on the merits.

Applicants respectfully submit that the amendment to claim 4 submitted herewith places claim 4 and claim 5, which depends from claim 4, in proper dependent form in compliance with 37 C.F.R. § 1.75(c). Applicants therefore respectfully request that the objection to claims 4 and 5 be withdrawn and submit that these claims can now be examined on the merits.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 1-3 and 10 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Rye et al. (*American Journal of Pathology* 150:99-106 (1997)). Specifically, the PTO asserts that Rye et al. teach a method for isolating tumor cells from blood, bone marrow,

ascitic or pleural fluids, and from enzyme-digested tissue biopsies, which method allegedly comprises filtering a suspension of cells through a 20-micron nylon microfilament filter to obtain a retained fraction of cells. The PTO further asserts that while Rye et al. teach an additional step (incubating cells with antibody bound to magnetic beads followed by magnetic separation of antibody-bound cells from cells not bound by antibody), Rye et al. teach that this step can be performed prior to filtration (Rye et al., page 13, lines 25-32).

Applicants respectfully traverse these grounds for rejection and submit that Rye et al. fail to anticipate the present claims. Applicants' invention is directed in pertinent part to a method for isolating disseminated tumor cells from a cell-containing body fluid, comprising passing the body fluid or part thereof that comprises a disseminated tumor cell through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen and are free from a separating agent that comprises a ligand for isolation. In another embodiment, the method comprises separating cellular components from non-cellular components in a body fluid that comprises a disseminated tumor cell to obtain a cell-containing fraction; resuspending the cell-containing fraction in a suspension medium; and passing the resuspended cell-containing fraction through a screen as recited to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen and are free from a separating agent that comprises a ligand for isolation. In certain embodiments, the ligand is an antibody or a lectin.

Applicants respectfully submit that Rye et al. fail to anticipate each and every limitation of the instant claims and, therefore, cannot be regarded as novelty-destroying. Rye et al. fail to teach or suggest that the disseminated tumor cells are free from a separating agent that comprises a ligand for isolation (*see, e.g.,* specification, page 19, lines 16-21). Instead, Rye et al. explicitly teach isolation of tumor cells using antibody-conjugated magnetic beads prior to a filtration step that retains cells attached to immunobeads on a filter (*see* Rye et al., Abstract; Introduction (last sentence); Methods (page 101); Results (page 102)). Rye et al. refer to the method described therein as "immunobead filtration," which permits the isolation of tumor cells using antibody-conjugated superparamagnetic beads (Rye et al., page 104, second column, lines 1-4). Therefore, Rye et al. fail to teach or suggest a method for isolating disseminated tumor

cells in which a disseminated tumor cell-containing body fluid is passed through a screen to separate non-cancer cells from disseminated tumor cells, such that the disseminated tumor cells are free from a separating agent that comprises a ligand used for isolation, such as an antibody-conjugated superparamagnetic bead. With regard to claim 3, Rye et al. also fail to teach or suggest separating cellular components from non-cellular components in the body fluid to obtain a disseminated tumor cell-containing fraction, which is resuspended and passed through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, nor do Rye et al. teach isolating the disseminated tumor cells from the body fluid such that the disseminated tumor cells are free from a separating agent that comprises a ligand for isolation (*e.g.*, an antibody). Applicants therefore respectfully submit that Rye et al. do not anticipate the present claims and request that the PTO withdraw this rejection.

The PTO also rejects claims 1-3 and 10 under 35 U.S.C. § 102(e), asserting lack of novelty. In particular, the PTO asserts that U.S. Patent No. 6,265,229-B1 (Fodstad et al.) teaches a method for isolating micrometastatic tumor cells from various bodily fluids, the method comprising filtering a suspension of cells through a porous membrane, preferably a membrane that has 20 micron pores, to obtain a retained fraction of cells. The PTO further asserts that a suspension of cells from blood and bone marrow may first be separated by density gradient centrifugation.

Applicants respectfully traverse these grounds for rejection and submit that Fodstad et al. fail to anticipate each and every limitation of the present claims. Fodstad et al. fail to teach or suggest a method for isolating disseminated tumor cells in which a disseminated tumor cell-containing body fluid is passed through a screen to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are retained on the screen and are free from a separating agent comprising a ligand for isolation, such as an antibody-conjugated particle. Instead, Fodstad et al. explicitly teach an "immunomagnetic method for detection of specific target cells" (*see* Fodstad et al., column 1, lines 12-15). The method described in Fodstad et al. requires attachment of antibodies directly to paramagnetic particles for use in separating target cells from non-target cells (*see, e.g.,* Fodstad et al., column 5, lines 57-65). After mixing the antibody-conjugated paramagnetic particles with a suspension of cells, the

mixture may be subjected to a filtering step to isolate the particles that have cells attached (*see, e.g.,* Fodstad et al., column 6, lines 25-35; column 8, lines 37-44). Fodstad et al. also therefore fail to teach or suggest separating cellular components from non-cellular components in the body fluid to obtain a disseminated tumor cell-containing fraction that is resuspended and passed through a screen having a mesh or pore width of about 15 to 30 μm to separate non-cancer cells from disseminated tumor cells, wherein the disseminated tumor cells are isolated free from a separating agent that comprises a ligand for isolation such as an antibody. Applicants therefore respectfully submit that Fodstad et al. do not anticipate the present claims.

Accordingly, Applicants submit that the subject matter of the present claims is novel, satisfying the requirements of 35 U.S.C. § 102. Applicants respectfully request that the PTO withdraw these rejections.

Applicants respectfully submit that all claims in the Application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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